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Outcomes of Gestational Trophoblastic Disease in King Khalid National Guard Hospital

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ABSTRACT

Objective: The objective of this study is to review the outcomes of gestational trophoblastic disease in our center, and to compare it with international figures. We will calculate the rates of remission, recurrence, and mortality. Also, we will determine the mean duration taken for normalization of ß-hCG level after initiation of treatment, and the distribution of the disease by age and parity.

Methods: Retrospective chart review of the patients diagnosed with gestational trophoblastic disease (GTD) and treated in King Khalid National Guard Hospital in the period between January 2000 and December 2005.

Results: During the study period, there were 29 cases of gestational trophoblastic disease. The majority of the cases were non-metastatic GTD (55.2%) followed by, in decreasing order of frequency, molar pregnancy (24.1%), metastatic high-risk GTD (10.3%), metastatic low-risk GTD (6.9%) and placental-site trophoblastic tumor (3.4%). Patient's age ranged from sixteen to fifty-three years old, with the majority in the fourth decade of life (37.9%). The parity as well was highly variable from zero to fifteen, with the majority between five and ten (37.9%). Remission rate in the malignant GTD was 85.7%. There were no cases of recurrence during the follow-up period. The overall mortality rate was 3.4%. The mean duration required for normalization of ß-hCG level was 10.3 weeks for molar pregnancy and 11.6 weeks for malignant GTD.

Conclusion: The chemotherapy success rate, remission rate & mortality rate were similar to that reported in earlier studies. There is a need for patient education regarding strict follow-up for early detection and intervention of malignant sequelae.

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INTRODUCTION

Epidemiology

Gestational trophoblastic disease (GTD) defines a heterogeneous group of interrelated lesions arising from the trophoblastic epithelium of the placenta. It is characterized by a distinct tumor marker, the beta subunit of human chorionic gonadotropin (hCG). The pathogenesis of GTD is unique because the maternal tumor arises from gestational rather than maternal tissue.

The incidence of GTD varies widely in different regions of the world (1). One reason for this variation is that epidemiologic data on GTD are limited by the rarity of the disease and inaccurate ascertainment of the number of gestational events in the population. As an example, the incidence has been inflated by not taking into account a large number of births that occurred at home or outside the referral center (2, 3).

The incidence of hydatidiform mole ranges from 0.2 to 2 cases per 1000 pregnancies, while malignant GTD is less common. North American and European countries tend to report low or intermediate rates of disease, whereas Asian and Latin American nations often have high rates. There is a twofold increased risk of GTD in Saudi Arabia and Japan. An epidemiological study conducted in Riyadh showed that the incidence of hydatiform mole is 1: 448 pregnancies while that of malignant counterpart is 1:6130 pregnancies (4). Another study was conducted in Al-Khobar showed that the incidence of hydatiform mole is 2.2:1000 deliveries with a 10% malignant sequalae (5).

Risk Factors

The most well-established risk factor for GTD is maternal age. The risk is significantly increased in those older than age 35, and slightly increased in those under age 20 [2]. Nevertheless, most cases of GTD occur in women under age 35 because of the greater number of pregnancies among younger women. This was supported by the study conducted in Al-Khobar where 68% of the cases were in the second and third decades of life (5).

History of previous GTD

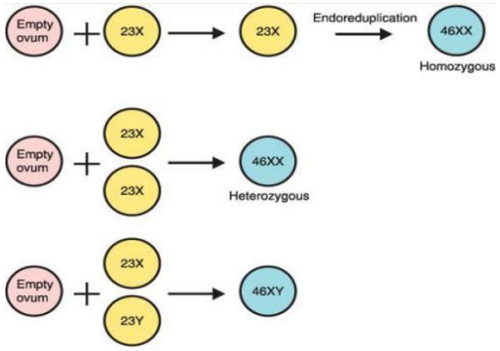
Studies from the United States and England have found that women with a history of one molar pregnancy (partial, complete, or persistent mole) have an approximately 1 percent chance of recurrence in subsequent pregnancies (compared to a 0.1 percent incidence in the general population of the United States). The recurrence rate is much higher after two molar pregnancies (16 to 28 percent).

Other risk factors that have been associated with GTD include current smoking (>15 cigarettes per day), maternal blood type AB, A, or B, history of infertility, nulliparity, and use of oral contraceptives (however, oral contraceptives do not increase the risk of developing postmolar GTD) (1). The mechanism for these associations has not been explained and increased risk has not been demonstrated consistently.

Pathology

There are several histological types of GTD (6, 7):

1. Hydatidiform mole (complete or partial): 80%
2. Persistent/invasive gestational trophoblastic neoplasia (GTN)
3. Choriocarcinoma
4. Placental site trophoblastic tumors



Cytogenetics of complete mole

Partial mole

They are usually (about 90 percent) triploid (69 XXX, 69 XXY, rarely 69 XYY) due to the fertilization of an ovum (one set of haploid maternal chromosomes) by two sperm (two sets of haploid paternal chromosomes). Flow cytometry studies have revealed a variety of other karyotypes in the remaining 10 percent. The fetal or embryonic tissue may have a normal diploid or a triploid karyotype.

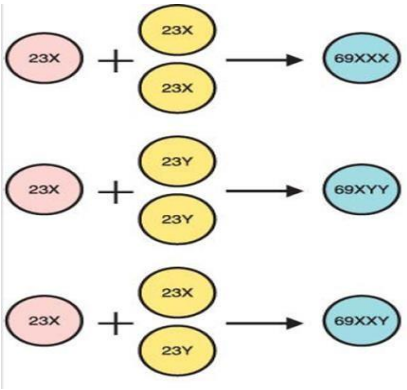
Complete and partial hydatidiform moles are differentiated by their karyotype, gross morphology, histologic appearance, and clinical features.

Cytogenetics

Chromosomal abnormalities are characteristic of all GTDs; assessment of DNA content enhances the diagnostic accuracy of histological diagnosis.

Complete mole

Usually has an apparently normal 46, XX karyotype, but both nuclear chromosomes are of paternal origin. This results from fertilization of an "empty" egg by a haploid sperm that then duplicates. A small number (3 to 13 percent) of complete moles have a 46, XY chromosome complement; this is thought to occur when an empty ovum is fertilized by two sperm. Because the nucleus is entirely paternal in origin, a complete mole is actually a paternal allograft in the mother. Aneuploidy can also occur. Rarely, complete moles are diploid and biparental. This karyotype seems to be found in patients with recurrent hydatiform mole and may be associated with an autosomal recessive condition that predisposes to molar pregnancy. This defect is likely due to dysregulation of genomic imprinting, in some cases related to a mutation at the 1.1 MB region on chromosome 19q13.4. In one series of 152 pregnancies among 37 women with familial recurrent mole, complete mole and partial moles occurred in 74 and 4 percent of pregnancies, respectively. A normal pregnancy developed in only 5 percent, the remainder were described as spontaneous abortions (17 percent).



Cytogenetics of partial mole

Histology

Hydatidiform moles are noninvasive proliferative processes associated with swelling of the villi. A major difference between the two types of molar pregnancy is that partial moles contain fetal/embryonic tissue and complete moles do not.

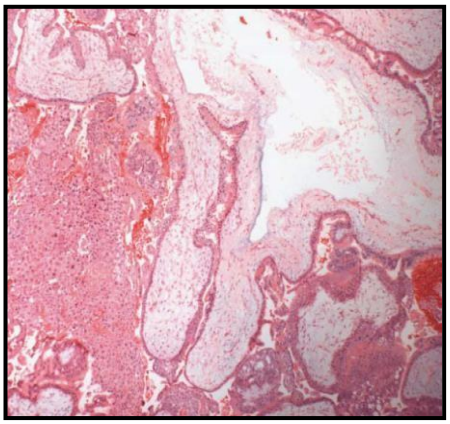
Complete mole: the chorionic villi of a complete mole are diffusely hydropic (vacuolar) and surrounded by hyperplastic, often atypical, trophoblast. No fetal tissue is present. However, twin pregnancy may be complicated by GTD: either a mole (complete or partial) and viable fetus or two moles. Expression of cytokeratin 20 (CK20) might help in distinguishing between

molar and normal trophoblastic tissue.

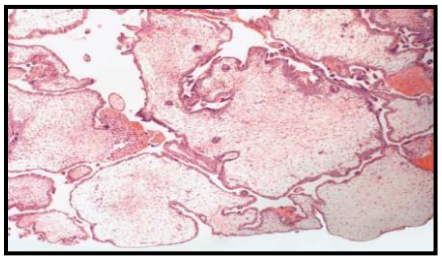
Partial mole

In contrast to complete mole, a partial mole may contain some normal appearing chorionic villi and fetal tissue. The hydropic changes are focal and less prominent with little hyperplasia and no atypia of the surrounding trophoblast. Marked scalloping of chorionic villi and trophoblastic stromal inclusions are also seen.

Histologically, 75 percent of cases of stable or serially rising serum beta-hCG concentrations after a molar pregnancy represent invasive moles and 25 percent are choriocarcinomas (placental site trophoblastic tumor is rare). In contrast, persistent elevation of serum beta-hCG following any nonmolar pregnancy is always due to choriocarcinoma or placental site trophoblastic tumor (rare) (6).



Histopathology of partial mole



Histopathology of complete mole

Invasive mole is characterized by the presence of enlarged hydropic villi with proliferation of trophoblast and the abnormal villi penetrate deeply into the myometrium. Histopathologically, these lesions may mimic choriocarcinoma with invasion of the uterine vasculature and the production of secondary metastatic lesions, particularly involving the vagina and lungs. However, unlike choriocarcinoma, an invasive mole may regress spontaneously.

Features of Complete and Partial Hydatidiform Moles

Feature	CompleteMoles	PartialMoles
Fetal or embryonictissue	Absent	Present
Hydatidiform swellingof chronic villi	Diffuse	Focal
Trophoblastichyperplasia	Diffuse	Focal
Trophoblastic stormalinclusions	Absent	Present
Genetic parentage	Paternal	Bipaternal
Karyotype	46XX; 46XY	69XXY; 69XYY
Persistent humanchorionic gonadotropin	20% ofcases	0.5% ofcases

Choriocarcinoma

It is a highly malignant epithelial tumor. It can arise from any type of trophoblastic tissue but only rarely occurs after a partial mole (6).

Most lesions begin in the uterus, although ectopic pregnancies provide extrauterine sites of origin. The most common sites of metastases are lung, brain, liver, pelvis, vagina, spleen, intestine, and kidney.

Histologically, choriocarcinoma appears as sheets of anaplastic cytotrophoblasts and syncytiotrophoblasts without chorionic villi. Some intermediate trophoblasts may also be seen. Extensive necrosis, hemorrhage, and vascular invasion are common.

Most choriocarcinomas follow molar pregnancies and are aneuploid. Postmolar choriocarcinoma is comprised exclusively of paternal DNA; choriocarcinoma following a normal gestation is comprised of biparental chromosomes identical to the fetus.

Placental site trophoblastic tumors

malignant neoplasms originating from intermediate cytotrophoblast cells. They occur months to years after a term gestation (but can develop after any type of pregnancy) and generally present microscopically as trophoblastic infiltration that is confined to the endometrium and myometrium of the placental implantation site.

On histological examination, there are no chorionic villi but, in contrast to choriocarcinoma, the typical dimorphic pattern of anaplastic cytosyncytiotrophoblasts is absent. Instead, there is a characteristic pattern consisting of mononuclear cells infiltrating the myometrium with proliferation of intermediate cytotrophoblast cells. Immunohistochemical staining for human placental lactogen (hPL) and placental alkaline phosphatase (PAP) are additional diagnostic tests for PSTT that have a specificity of approximately 60 percent. In addition, high proliferative activity (as assessed by Ki-67 staining) and positive staining for alpha-inhibin and cytokeratin 8/18 and negative smooth muscle markers confirm the diagnosis of PSTT.

Pathogenesis of GTD

Why excess paternal chromosomes result in GTD is not known. However, the presence of Y chromatin appears to be related to the potential for malignant growth. This was illustrated in a study that detected Y chromatin in only 9 percent of hydatidiform moles, but 50 percent of invasive moles, and 74 percent of choriocarcinomas.

Several studies have described interesting molecular pathways that might contribute to the development of GTD. Somatic point mutations and instability of mitochondrial DNA were found in samples of hydatiform moles and choriocarcinoma. Amplification and overexpression of various oncogene products, such as c-erbB-2, have been shown to be associated with a higher proliferation index and more aggressive behavior in GTDs. Downregulation of tumor suppressor genes, including p53 and Rb, has also been demonstrated in GTD.

Clinical Manifestations

Clinical manifestations of GTD include, in decreasing order of frequency:

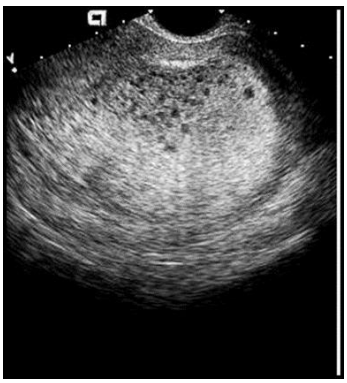
- Vaginal bleeding
- Enlarged uterus
- Pelvic pressure or pain
- Theca lutein cysts
- Anemia
- Hyperemesis gravidarum
- Hyperthyroidism
- Preeclampsia before 20 weeks of gestation
- Vaginal passage of hydropic vesicles

Clinicians most often initially suspect a pregnancy complication (threatened or missed abortion, ectopic pregnancy) rather than GTD in women who present with vaginal bleeding, an enlarged uterus, and pelvic discomfort and have a positive pregnancy test.

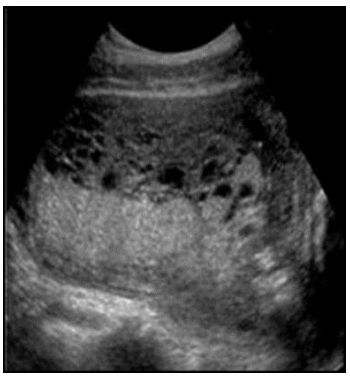
Management

Initial work-up includes ß-hCG, complete blood count, renal function test, liver function test, thyroid function test, blood group, chest X-ray and pelvic ultrasound.

Initial management of suspected complete or partial mole is evacuation of the uterine contents by suction curettage (8). Evacuation is indicated for pathologic confirmation of the diagnosis, relief of symptoms, and to prevent complications related to molar pregnancy. This procedure is a definitive therapy for most patients. Patients who have no desire for future fertility may opt for hysterectomy, which eliminates the risk of local invasion, but does not prevent metastasis. The adnexae may be retained in these cases.



Ultrasounds of complete mole



Ultrasounds of partial mole

The goal of the treatment and follow-up of hydatiform moles is to avoid transformation into a frankly malignant condition which can be deadly if left untreated. 18 – 28% of patients with complete mole will develop persistent neoplasia (6). In contrast, following partial molar pregnancy, the risk of persistent GTN is 2 – 4%. Patients are followed with weekly ß-hCG levels until three consecutive normal values are obtained. Historically, patients with complete and partial molar pregnancy were then followed with monthly ß-hCG levels for a total of six months. Approximately 50% of patients had normal ß-hCG levels between 6 and 14 weeks after molar evacuation (9). Non-compliance with recommended follow-up is common. Investigators have begun to question whether the follow-up period could safely be shortened. One such study of 1029 women at the New England Trophoblast Disease Center (NETDC) with complete molar pregnancy reported that no persistent disease occurred among patients with spontaneous regression of ß-hCG levels to < 5 mIU/ml (10). Another study of women with partial molar pregnancy reported that none of 238 women with complete follow-up and spontaneously declining ß-hCG levels developed persistent disease after reaching undetectable levels (11). Theoretically, follow-up could be shortened for 97% of patients (10).

Metastatic work-up and chemotherapy are needed in any patient with rising or plateauing ß-hCG; detected metastasis by history or examination and histopathplogical finding of invasive mole, choriocarcinoma or placental site trophoblastic tumor.

Staging

For most patients with malignant diseases, outcome stratification and selection of appropriate therapy is based upon the anatomic extent of disease, which in turn, determines

the disease "stage". Compared with other malignancies, malignant GTD is unique in that prognosis is dependent upon other factors, such as serum beta-hCG concentration, in addition to disease extent. Further, in most cases, the diagnosis is based upon clinical and biochemical parameters; histologic confirmation and surgical staging may not be obtained. Finally, metastatic spread to distant organs, in particular the lungs, can occur early, even in the absence of disease in the uterus or pelvis. There are several staging or classification systems for GTD. The most useful one for clinical practice is the NCI/NIH clinical classification:

1. Benign GTD:
2. complete mole
3. partial mole
4. Malignant GTD:
5. non-metastatic GTD
6. metastatic GTD: good prognosis (low risk) & poor prognosis (high risk), depending on the presence of any of the following risk factors:
   a. duration of the disease > 4 months
   b. pretherapy ß -hCG > 40,000IU/ml
   c. brain or liver metastases
   d. GTD after term gestation
   e. prior failed chemotherapy

The International Federation of Gynecologists and Obstetricians (FIGO) initially developed a four-tiered anatomic staging system for GTN based upon disease distribution:

- Stage I: All patients with persistently elevated beta-hCG levels and those with tumors confined to the uterus.
- Stage II: All patients with tumor outside of the uterus, but localized to the vagina and/or pelvis.
- Stage III: Pulmonary metastases with or without uterine, vaginal or pelvic involvement.
- Stage IV: Patients with metastases involving the brain, liver, kidneys, or gastrointestinal tract.

All stages were further stratified as A, B or C depending on the presence or absence of one or both of two risk factors for recurrence (beta-hCG ≥100,000 IU in a 24-hour urine collection, or the detection of disease more than 6 months followed termination of an antecedent pregnancy.

Clinical or prognostic staging evolved when it was recognized that the selection of treatment in GTN should not only be affected by anatomic site, but also by a number of clinical and prognostic factors that influence risk. In 2002, FIGO approved a revision of the staging system for GTN that was subsequently adopted by the American Joint Committee on Cancer in its 2002 staging manual. The basic FIGO stages I to IV were retained to describe the anatomic site(s) of disease, but the prior A, B, and C risk modifier subgroups were eliminated, and replaced by a modification of the World Health Organization (WHO) scoring system called the Prognostic Scoring Index.

The World Health Organization Scoring System (the Prognostic Scoring Index) 2002

FIGO Score	0	1	2	4
Age	≤ 39	>39		
Antecedent pregnancy	Hydatidiform mole	Abortion	Term pregnancy	
Interval from index pregnancy (months)	<4	4–6	7–2	>12
Pretreatment ß-human chorionic gonadotropin (mIU/mL)	<1000	1000–10,000	>10,000-100,000	>100,000
Largest tumor size including uterus (cm)	3–4	5		
Site of metastases	Lung	Spleen, kidney	GI tract	Brain, liver
Number of metastases identified	0	1–4	5–8	>8
Previous failed chemotherapy			Single drug	Two or more drugs
Score value: ≤6 = low risk; ≥7 = high risk.				

Compared to earlier versions, this modified scoring system eliminated blood group type as a risk factor, and upgraded liver metastases from score 2 to 4.

In addition to its prognostic utility, the revised FIGO staging system is capable of predicting which patients are likely to respond poorly to single-agent chemotherapy, and thus can be used to help select appropriate treatment protocols. A prognostic score of 7 or higher is considered a high risk score, and these patients all require combination chemotherapy. Patients with scores under 7 are considered low-risk, and can usually be managed using single-agent chemotherapy.

The prognostic score adds little to the selection of treatment for women with FIGO stage I and stage IV disease. In general, women with FIGO stage I disease generally have low-risk scores, and over 90 percent achieve remission with single agent chemotherapy. In contrast, patients with FIGO stage IV disease have high risk scores, and are most likely to be resistant to single-agent chemotherapy. Most of these patients have the histologic pattern of choriocarcinoma following a nonmolar pregnancy; they often have a delayed diagnosis and large tumor burden.

Thus, the benefit of using the prognostic score to distinguish between clinically high-risk and low-risk disease applies primarily to women with FIGO stage II and III disease.

GTTs are the first and only disseminated solid tumours that have proved to be highly curable by chemotherapy which is the prime modality of treatment for choriocarcinoma and invasive mole. The remission rate of good prognosis metastatic GTT by chemotherapy is approximately 90%. Unlike choriocarcinoma and invasive mole, PSTT is relatively chemo-resistant, although case reports of complete remissions in response to combination therapy with EMA and EMA-CO have been published.

Single agent chemotherapy is indicated for treatment of non-metastatic and good-prognosis GTD. Methotrexate or

dactinomycin achieves a 95% remission. If this fails, salvage with the alternative single agent. If both fail, use EMA/CO (etoposide, methotrexate, dactinomycin/ cyclophosphamide & onconovin) or MAC (methotrexate, dactinomycin, chlorabucil).

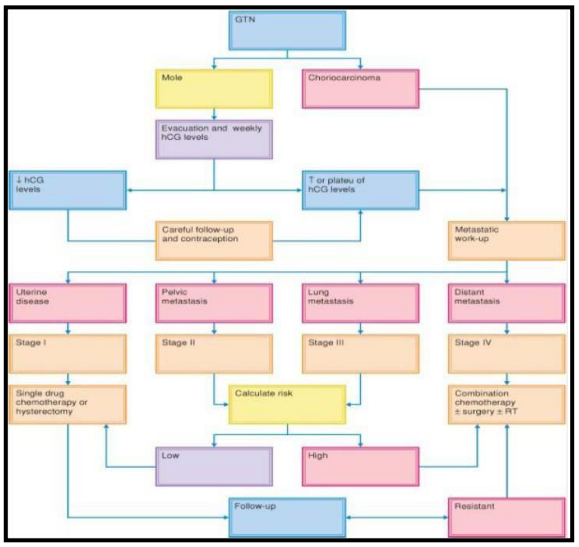
Poor-prognosis metastatic GTD requires combination chemotherapy front-line (EMA/CO). Salvage treatment can use EMA/EP (etoposide, methotrexate, dactinomycin/ etoposide & platinum). In one series of 272 women with high risk GTN who were treated with EMA/CO, 78% entered remission & 17% developed resistance to EMA/CO (12). Another study showed that the ß-hCG titer decreased 69.8% in EMA/CO regimen with a remission rate of 90.6% (87/96) and the number of courses of chemotherapy until remission was 8.5 + /-2.2(13).

The patient is considered in remission after 3 consecutive weekly negative ß-hCG titers (<5IU/ml). After remission, follow-up every month is required for 1year to watch for recurrence. The overall risk of recurrence after 1year of remission is <1%. Some centers continue biannual titers indefinitely for high risk individuals, although 85 – 95% of recurrences, which are detected as new elevations in serum ß-hCG, occur within the first 18 months (14).

Contraception

It is essential that women use contraception both during and for the entire duration of gonadotropin follow-up [8]. Oral contraceptives are preferred. Pregnancy should be avoided for at least one year following treatment for GTN, as it can lead to difficulty with interpretation of ß-hCG levels. Studies have shown, however, that women who do conceive before one year generally have a good prognosis [15]. Chemotherapy does not generally have an adverse effect on future fertility, the rate of spontaneous abortion or congenital malformations with future pregnancies, or child development following a subsequent term pregnancy (15).

Management scheme of GTN



MATERIALS AND METHODS

Retrospective chart review was done for the patients who were diagnosed with gestational trophoblastic disease (GTD) and treated in KKNGH in the period between January, 2000 and December, 2005.

Data were analyzed with SPSS statistical software. Results were displayed in terms of frequency, mean and median as appropriate.

RESULTS

During the study period there were 29 cases of gestational trophoblastic disease. Eleven cases (37.9%) were diagnosed and treated primarily in King Khalid National Guard Hospital, while the remaining eighteen patients (62.1%) were referred from other hospitals for further management (Table 1).

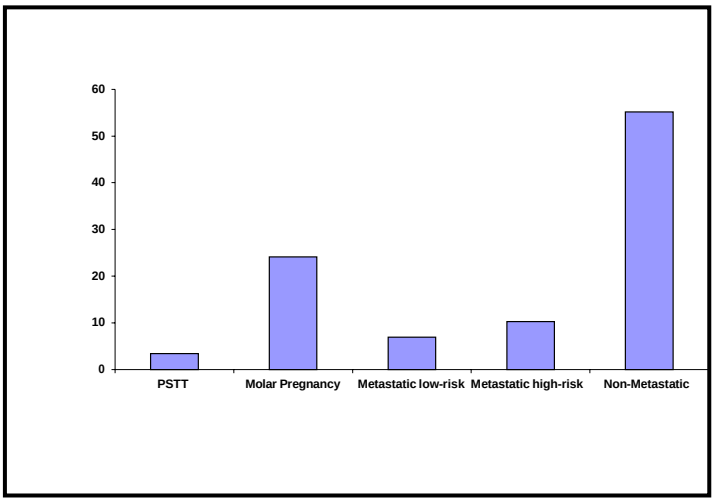
Table 1: Primary place of presentation

Place	Frequency	%
Diagnosis in KKNGH	11	37.9
Referral	18	62.1
Total	29	100.0

Majority of the cases were non-metastatic GTD (55.2%) followed by; in decreasing order of frequency; molar pregnancy (24.1%), metastatic high-risk GTD (10.3%), metastatic low-risk GTD (6.9%) and placental-site trophoblastic tumor (3.4%). Table 2 & graph 1.

Table 2: Classification of the disease

Recurrence	Frequency	%
Placental-site trophoblastic tumor (PSTT)	1	3.4
Molar Pregnancy	7	24.1
Metastatic low-risk GTD	2	6.9
Metastatic high-risk GTD	3	10.3
Non-Metastatic GTD	16	55.2
Total	29	100.0

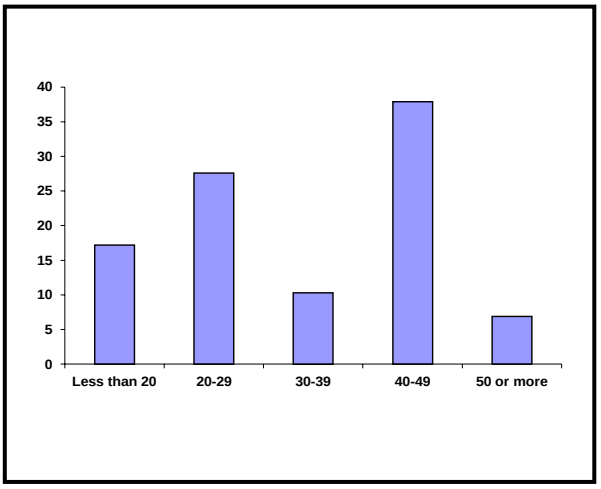


Graph 1: Classification of the disease

The age was variable from sixteen to fifty-three years old with the majority in the fourth decade of life (37.9%) followed by the second decade (27.6%). Table 3 & graph 2.

Table 3: Age-distribution of the disease

Age	Frequency	%
Less than 20	5	17.2
20-29	8	27.6
30-39	3	10.3
40-49	11	37.9
50 or more	2	6.9
Total	29	100.0

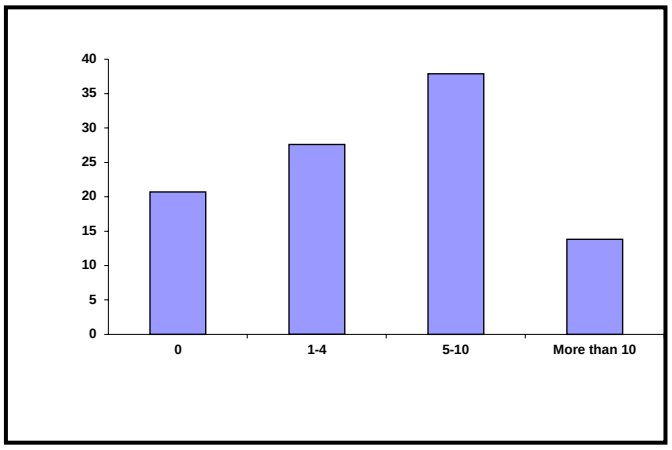


Graph 2: Age-distribution of the disease

The parity as well was highly variable from zero to fifteen with the majority between five and ten (37.9%). Table 4 & graph 3.

Table 4: Parity-distribution of the disease

Parity	Frequency	%
0	6	20.7
1-4	8	27.6
5-10	11	37.9
More than 10	4	13.8
Total	29	100.0



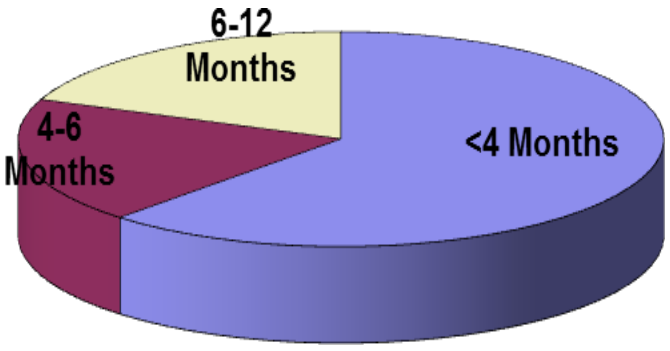
Graph 3: Parity-distribution of the disease

Among the seven cases of molar pregnancy, the mean age of presentation was 23 and the mean parity was 1.4. The mean hemoglobin level at the time of presentation was 11.4 g/dl. The ß-hCG level was ranging from 41220 mIU/ml to more than 200000 mIU/ml with a median of 145306 mIU/ml. All of the patients underwent suction curettage. One patient (14.3%) required re-evacuation for persistent vaginal bleeding. No other interventions were required such as blood transfusion, hysterectomy or uterine artery embolization. One patient (14.3%) lost follow-up completely after the evacuation. The remaining six patients (85.7%) were following on weekly basis until normalization of their ß-hCG levels. The mean duration taken for normalization of ß-hCG level was approximately 10.3 weeks. No recurrence was observed even in the three patients who got pregnant within six months of normalization of ß-hCG level.

There were 21 patients with malignant gestational trophoblastic disease, accounting for 72.4% of the total number of patients. The mean age of presentation was 36.6 and the median parity is 6.6. they were sub-classified as follows: 16 patients with non-metastatic GTD (76.2%), 2 patients with metastatic low-risk GTD (9.5%) and 3 patients with metastatic high-risk GTD (14.3%). 20 cases were preceded by molar pregnancy (95.2%) and one case was preceded with preterm birth (4.8%). No cases were preceded by abortion, ectopic or term gestations. Chemotherapy was initiated within 4 months of previous pregnancy in 13 patients (61.9%), between 4 and 6 months in 4 patients (19%), between 6 and 12 months in 4 patients (19%) and after 12 months in none of them. Table 5& graph 4.

Table 5: Interval between antecedent pregnancy and initiation of chemotherapy

Antecedent Pregnancy	Frequency	%
<4 Months	13	61.9
4-6 Months	4	19.0
6-12 Months	4	19.0
>12 Months	0	0.0
Total	21	100.0



Graph 4: Interval between antecedent pregnancy and initiation of chemotherapy

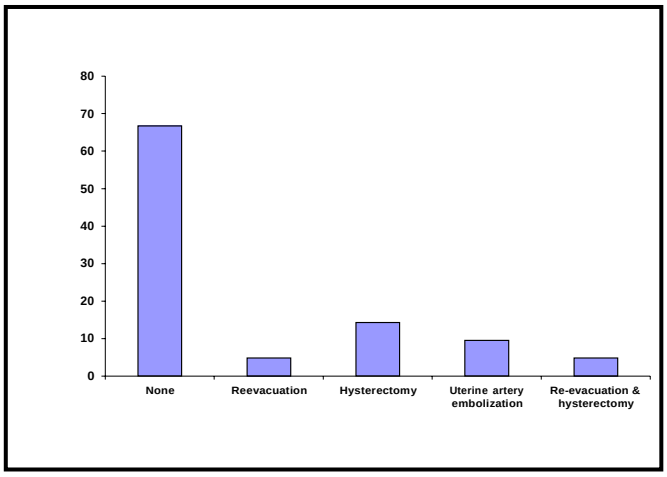
Four patients (19%) were started on chemotherapy in another hospital before their referral to our institute. Fourteen patients (66.7%) were treated solely with single-agent chemotherapy. Seven patients (33.3%) required multiple-agent chemotherapy, three of them initially were treated with single-agent chemotherapy. Eighteen patients (85.7%) completed treatment with normalization of ß-hCG level. In three patients ß-hCG level did not drop to the normal value; as one of them lost the follow-up, one of them is still on treatment currently and the last patient died from the disease. Thus, the overall mortality rate was 3.4%. Sixteen patients (88.9%) of those who completed the

treatment had follow-up for more than twelve months while two patients (11.1%) had follow-up for six to twelve months. No single case of recurrence was found during the follow-up period.

Regarding the frequency of interventions; one patient (4.8%) required re-evacuation, three patients (14.3%) required hysterectomy, two patients (9.5%) required uterine artery embolization, one patient (4.8%) required both re-evacuation and hysterectomy. Majority of the patients (66.7%) did not require any intervention. Table 6 & graph 5.

Table 6: Frequency of co-interventions

Co-Intervention	Frequency	%
None	14	66.7
Re-evacuation	1	4.8
Hysterectomy	3	14.3
Uterine artery embolization	2	9.5
Re-evacuation & Hysterectomy	1	4.8
Total	21	100.0



Graph 5: Frequency of co-interventions

The mean number of chemotherapy cycles was 5.3 for single-agent chemotherapy, 6.1 for multiple-agent chemotherapy and 6.6 for both. The mean duration required for normalization of ß-hCG level was 11 weeks for single-agent chemotherapy, 13 for multiple-agent chemotherapy and 11.6 for both. The median pre-treatment ß-hCG level was 5760 mIU/ml.

There was one case of placental-site trophoblastic tumor among the 29 cases. It was managed by total abdominal hysterectomy with bilateral salpingo-oophorectomy. It was diagnosed by histopathological evaluation. No recurrence occurred during the follow-up period.

DISCUSSION

There were a small number of patients as the disease is rare, but this was comparable to other studies conducted on the same topic. Also, there were a higher proportion of malignant GTD (72.4%) as our hospital is one of the gyne-oncology referral centers. The remission rate for malignant GTD was 85.7% for both single and multiple-agent chemotherapy. This result was comparable to previous studies which showed a remission rate of 78% to 95%. For the patients who achieve remission, there were no cases of recurrence. The mean duration of normalization of ß-hCG level was reported to be 6 to 14 weeks, while in our study; it was 10.3 weeks for molar pregnancy and 11.6 weeks for malignant GTD. There was a single case of mortality among the studied population which accounts for 4.3%. This case was assigned to the high-risk metastatic group and was treated initially in two other hospitals with multiple courses of chemotherapy. Chemo-resistance occurred secondary to poor compliance.

CONCLUSION

There were a small number of patients as the disease is rare, but this was comparable to other studies conducted on the same topic. Also, there were a higher proportion of malignant GTD (72.4%) as our hospital is one of the gyne-oncology referral centers. The remission rate for malignant GTD was 85.7% for both single and multiple-agent chemotherapy. This result was comparable to previous studies which showed a remission rate of 78% to 95%. For the patients who achieve remission, there were no cases of recurrence. The mean duration of normalization of ß-hCG level was reported to be 6 to 14 weeks, while in our study; it was 10.3 weeks for molar pregnancy and 11.6 weeks for malignant GTD. There was a single case of mortality among the studied population which accounts for 4.3%. This case was assigned to the high-risk metastatic group and was treated initially in two other hospitals with multiple courses of chemotherapy. Chemo-resistance occurred secondary to poor compliance. In order to prevent such

occurrence, patients' education about the disease pathology and complications is essential. Strict follow-up on weekly basis with ß-hCG level is important. At least three consecutive normal values are needed for molar pregnancy, while follow-up at monthly intervals for six to twelve months thereafter are required for malignant GTD. In this way, malignant sequelae are detected and managed earlier and thus cure will be ultimate outcome.

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Not applicable

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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